PATENT
Docket No. 337462000600
Client Reference BMID 9619/US

16/C

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Mei Leung

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Mark M. RICHTER, *et al.*

Serial No.: 09/074,472

Filing Date: May 7, 1998

For: ASSAYS EMPLOYING ELECTROCHEMILUMINESCENT LABELS AND ELECTROCHEMILUMINESCENCE QUENCHERS

Examiner: A. Chakrabarti

Group Art Unit: 1655

AMENDMENT UNDER 37 C.F.R. § 1.111

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

This Amendment is in response to the Office Action mailed December 6, 1999 in the above-identified application, for which a response was due on March 6, 2000. A Petition for a one month extension of time is enclosed, thus extending the due date for response to April 4, 2000. Reconsideration of the application in view of the following amendments and remarks is respectfully requested.

Please amend the above-referenced application as follows:

AMENDMENTS

In the claims

Please cancel claim 24.

Please amend claims 1 and 25 as follows:

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1. (Twice Amended) A method for qualitative or quantitative electrochemiluminescence (ECL) detection of an analyte in a sample composition comprising the steps of:

(a) preparing an assay mixture comprising:

said sample composition;

a reagent having an ECL label, wherein said ECL label and said analyte are not identical; and,

a reagent having an ECL quenching moiety, said ECL ~~quenching moiety~~ comprising at least one benzene moiety, and wherein said ECL quenching moiety and said analyte are not identical;

(b) determining any difference between the ECL emissions of:

(i) the assay mixture prepared in step (a); and,

(ii) an assay mixture comprising:

said reagent having an ECL label;

said reagent having an ECL quenching moiety; and,

a known amount of said analyte; and,

(c) correlating any difference determined in step (b) with the amount of analyte in said sample.

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25. (Twice Amended) An assay reagent for use in the method according to claim 1, said assay reagent comprising the ECL quenching moiety of claim 1 and an ECL label,

wherein said ECL quenching moiety and said ECL label are not identical, said assay reagent provided in a suitable container.

REMARKS

With entry of the above amendments, claims 1-23 and 25-27 are pending in the application. Claim 24 has been canceled to promote prosecution, without disclaimer of any previously claimed subject matter. Claims 1 and 25 have been amended to promote prosecution of the application, without disclaimer of any previously claimed subject matter. A copy of the claims as amended is provided for the Examiner's convenience in the attached Appendix A. Support for the amendments appears throughout the specification and claims, for example, in Example 13 on pp. 61-64 of the specification, which describes an analyte (oligonucleotide) labeled with an ECL label ($Ru(bpy)_3^{+2}$) and an ECL quenching moiety (benzoquinone). Although the ECL label and ECL quenching moiety can both be attached to the analyte, the ECL label, ECL quenching moiety and analyte are not identical. No new matter has been introduced.

The Examiner indicated in a telephone conversation on March 21, 2000 that the Sequence Listing errors were corrected by STIC.

Rejections Under 35 U.S.C. § 102(b)

Claims 1, 2, 4, 9, 19-21, 24 and 25 are rejected under 35 U.S.C. § 102(b) as being anticipated by Chmura *et al.* (Journal of Biolumin Chemilumin (1994), Vol. 9, pp. 1-6). Claim 24 has been canceled. Applicants submit that claims 1, 2, 4, 9, 19-21 and 25 as amended are not anticipated by Chmura *et al.*.

Chmura *et al.* relates to the luminescence of anthracene-sensitized sodium citrate-methanol-dissolved O_2 solution, and its application for the determination of antioxidants. Chmura *et al.* describes an assay for the determination of kinetic parameters of antioxidants, which act as quenchers of anthracene-sensitized citrate-methanol electrochemiluminescence

(Table 1). The Examiner asserts that Chmura *et al.* discloses an analyte, which is anthracene (page 3 lines 5-6). Chmura *et al.* discloses an assay system in which the antioxidant acts as both the analyte and the quencher. Applicants submit that anthracene is not an analyte, but is part of the ECL label. Chmura *et al.* states that "addition of anthracene (0.1-10 mmol/L) to the electrolyte increased the light intensity (Fig. 3) approximately 10-50-fold owing to the electronic excitation energy transfer from primary excited species -- energy donors (P*) to anthracene -- an energy acceptor (A) (sensitized ECL)" (page 2). Further, as noted by the Examiner, "Chmura *et al.* teaches a method wherein said ECL label comprises a polyaromatic hydrocarbon (Table 1)."

Chmura *et al.* does not disclose a method for qualitative or quantitative ECL detection of an analyte, wherein the ECL label and the analyte are not identical, and wherein the ECL quenching moiety and the analyte are not identical, as described in claim 1. Further, Chmura *et al.* does not disclose an assay reagent for use in the method according to claim 1, said assay reagent comprising the ECL quenching moiety of claim 1 and an ECL label, wherein said ECL quenching moiety and said ECL label are not identical, said assay reagent provided in a suitable container, as defined by claim 25. Claims 2, 4, 9 and 19-21 depend from claim 1, and are not disclosed by Chmura *et al.*.

It is submitted that Chmura *et al.* does not identically disclose the claimed subject matter. Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. § 102(b) be withdrawn.

Claim 24 is rejected under 35 U.S.C. § 102(b) as being anticipated by Sigma Chemical Company (Catalog 1995). Claim 24 has been canceled without prejudice.

Rejections Under 35 U.S.C. § 103(a)

Claims 1-6, 9, 19-21 and 24-27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chmura *et al.* in view of Papalambros *et al.* (Journal of Photochemistry (1987), Vol. 39, pp. 85-96). Claim 24 has been canceled. Applicants submit that claims 1-6, 9,

19-21 and 25-27 as amended are not unpatentable over Chmura *et al.* and Papalambros *et al.*, alone or in combination.

As described above, Chmura *et al.* does not disclose claim 1, or dependent claims 2, 4, 9, 19-21, and 25. Claims 3, 5, 6, 26 and 27 also depend from claim 1. The Examiner notes that Chmura *et al.* does not teach a method wherein the quenching moiety comprises at least one phenol moiety, at least one benzene carboxylic acid moiety or at least one benzene carboxylate moiety, as defined in claims 3, 5 and 6, respectively. As noted by the Examiner on page 8, Chmura *et al.* does not teach the motivation to combine all the reagents for detecting an analyte in a sample in the form of a kit, as described in claims 26 and 27.

Nothing in Chmura *et al.*, in view of Papalambros *et al.*, suggests the claimed methods or compositions. Papalambros *et al.* discloses rate constants for the quenching of the fluorenone fluoresence by substituted benzaldehydes and benzoic acids. Papalambros *et al.* does not disclose a method for qualitative or quantitative ECL detection of an analyte, as described in claim 1. Papalambros *et al.* also does not disclose combining all the reagents for detecting an analyte in a sample in the form of a kit, as described in claims 26 and 27. There would be no motivation to combine the quenchers of Papalambros *et al.* with the assay of Chmura *et al.*, since Chmura *et al.* relates to a system suitable for the assay of the concentration and kinetic parameters of free radical scavengers, especially biologically active, lipid soluble antioxidants. The claimed methods and compositions are not suggested by the disclosure of Chmura *et al.*, alone or in combination with Papalambros *et al.*.

Claims 1, 2, 4, 7-9, 19-21, 24 and 25 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chmura *et al.* in view of Gudibande *et al.* (PCT International Publication Number WO 93/12256). Claim 24 has been canceled. Applicants submit that claims 1, 2, 4, 7-9, 19-21 and 25 as amended are not unpatentable over Chmura *et al.* and Gudibande *et al.*, alone or in combination.

As described above, Chmura *et al.* does not disclose claim 1, or dependent claims 2, 4, 9, 19-21 and 25. Claims 7 and 8 also depend from claim 1. Further, as noted by the Examiner, Chmura *et al.* does not teach the method wherein said ECL label comprises ruthenium or osmium, as described in claims 7 and 8, respectively.

Nothing in Chmura *et al.*, in view of Gudibande *et al.*, suggests the claimed methods or compositions. Gudibande *et al.* discloses electrochemiluminescent labels for oligonucleotides using phosphoramidite chemistry. Gudibande *et al.* does not disclose a method for qualitative or quantitative ECL detection of an analyte, wherein the assay mixture comprises a reagent having an ECL quenching moiety, as described in claim 1. There would be no motivation to include the ECL label comprising ruthenium or osmium of Gudibande *et al.* with the method of Chmura *et al.*, which system was proposed as a model of the peroxidation of lipids in biomembranes.

Claims 1, 2, 4 and 9-27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chmura *et al.* in view of IGEN Catalog (1996). Claim 24 has been canceled. Applicants submit that claims 1, 2, 4, 9-23 and 25-27 as amended are not unpatentable over Chmura *et al.* and IGEN Catalog, alone or in combination.

As described above, Chmura *et al.* does not disclose claim 1, or dependent claims 2, 4, 9, 19-21 and 25-27. Claims 10-18, 22, 23 also depend from claim 1. As noted by the Examiner, Chmura *et al.* does not teach the method wherein the analyte comprises an oligonucleotide, DNA, RNA, polypeptide, antibody, antigen, an enzyme, an enzyme substrate or a polysaccharide, as claimed in claims 10-18, respectively, nor does Chmura *et al.* teach the method comprising the step of conducting a chemical reaction on a substrate present in an initial sample composition to produce said analyte in said sample composition either in step (a) or prior to step (a) before the determination of step (b), as described in claims 23 and 22.

Nothing in Chmura *et al.*, in view of IGEN Catalog, suggests the claimed methods or compositions. IGEN Catalog discloses ECL assays for the detection of JC virus, interleukin 8, and murine IgG. IGEN Catalog does not disclose a method for qualitative or quantitative ECL

detection of an analyte, wherein the assay mixture comprises a reagent having an ECL quenching moiety, as described in claim 1. There is no motivation from the applied publications, alone or in combination, to provide a method for ECL detection of an analyte, comprising preparing an assay mixture which comprises a sample composition, a reagent having an ECL label, wherein the ECL label and the analyte are not identical, and a reagent having an ECL quenching moiety, wherein the ECL quenching moiety and the analyte are not identical, as claimed.

Claims 1, 2, 4, 9, 19-21 and 24-27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chmura *et al.* in view of Stratagene Catalog (1988, p. 39). Claim 24 has been canceled. Applicants submit that claims 1, 2, 4, 9, 19-21 and 25-27 as amended are not unpatentable over Chmura *et al.* and Stratagene Catalog, alone or in combination.

As described above, Chmura *et al.* does not disclose the subject matter of claims 1, 2, 4, 9, 19-21 and 25-27. As noted by the Examiner on page 8, Chmura *et al.* does not teach the motivation to combine all the reagents for detecting an analyte in a sample in the form of a kit, as described in claims 26 and 27.

In combination with Stratagene Catalog, there still no suggestion of the claimed methods and compositions. Stratagene Catalog describes kits for gene characterization. Stratagene Catalog does not disclose methods or compositions for the ECL detection of an analyte. Neither Chmura *et al.* nor Stratagene Catalog, alone or in combination, suggest a method for ECL detection of an analyte, comprising preparing an assay mixture which comprises a sample composition, a reagent having an ECL label, wherein the ECL label and the analyte are not identical, and a reagent having an ECL quenching moiety, wherein the ECL quenching moiety and the analyte are not identical, as claimed. There is also no suggestion in the applied publications, alone or in combination, of assay reagent kits for use in the method according to claim 1, as described in claims 26 and 27.

Applicants therefore request that the rejections under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

Applicants submit that each of the claims as amended are novel and unobvious over the applied publications. Withdrawal of the outstanding rejections and allowance of each of the claims as amended herein is therefore respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 337462000600. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: April 4, 2000

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Appendix A
Claims as Amended

1. (Twice Amended) A method for qualitative or quantitative electrochemiluminescence (ECL) detection of an analyte in a sample composition comprising the steps of:

(a) preparing an assay mixture comprising:

said sample composition;

a reagent having an ECL label, wherein said ECL label and said analyte are not identical; and,

a reagent having an ECL quenching moiety, said ECL quenching moiety comprising at least one benzene moiety, and wherein said ECL quenching moiety and said analyte are not identical;

(b) determining any difference between the ECL emissions of:

(i) the assay mixture prepared in step (a); and,

(ii) an assay mixture comprising:

said reagent having an ECL label;

said reagent having an ECL quenching moiety; and,

a known amount of said analyte; and,

(c) correlating any difference determined in step (b) with the amount of analyte in said sample.

2. The method according to claim 1, wherein said ECL quenching moiety comprises at least one moiety selected from the group consisting of phenol moieties, quinone moieties, benzene carboxylic acid moieties, and benzene carboxylate moieties.

3. The method according to claim 1, wherein said ECL quenching moiety comprises at least one phenol moiety.

4. The method according to claim 1, wherein said ECL quenching moiety comprises at least one quinone moiety.

5. The method according to claim 1, wherein said ECL quenching moiety comprises at least one benzene carboxylic acid moiety.

6. The method according to claim 1, wherein said ECL quenching moiety comprises at least one benzene carboxylate moiety.

7. The method according to claim 1, wherein said ECL label comprises ruthenium.

8. The method according to claim 1, wherein said ECL label comprises osmium.

9. The method according to claim 1, wherein said ECL label comprises a polyaromatic hydrocarbon.

10. The method according to claim 1, wherein said analyte comprises an oligonucleotide.

11. The method according to claim 1, wherein said analyte comprises DNA.

12. The method according to claim 1, wherein said analyte comprises RNA.

13. The method according to claim 1, wherein said analyte comprises a polypeptide.

14. The method according to claim 1, wherein said analyte comprises an antibody.

15. The method according to claim 1, wherein said analyte comprises an antigen.

16. The method according to claim 1, wherein said analyte comprises an enzyme.

17. The method according to claim 1, wherein said analyte comprises an enzyme substrate.

18. The method according to claim 1, wherein said analyte comprises a polysaccharide.

19. The method according to claim 1, wherein said known amount of analyte is zero.

20. The method according to claim 1, wherein said reagent having an ECL label and said reagent having an ECL quenching moiety are the same reagent.

21. The method according to claim 1, wherein said reagent having an ECL label and said reagent having an ECL quenching moiety are different reagents.

22. The method according to claim 1, further comprising the steps of:

conducting a chemical reaction on a substrate present in an initial sample composition to produce said analyte in said sample composition prior to step (a); and,

correlating any difference determined in step (b) with the amount of substrate in said initial sample composition.

23. The method according to claim 1, further comprising the step of:

conducting a chemical reaction with the assay mixture prepared in step (a) before the determining of step (b).

24. (Cancelled)

25. (Twice Amended) An assay reagent for use in the method according to claim 1, said assay reagent comprising the ECL quenching moiety of claim 1 and an ECL label, wherein said ECL quenching moiety and said ECL label are not identical, said assay reagent provided in a suitable container.

26. An assay reagent kit for use in the method according to claim 1, said assay reagent kit comprising an assay reagent in a suitable container, said assay reagent comprising the ECL quenching moiety of claim 1, and instructions for performing said method.

27. An assay reagent kit for use in the method according to claim 1, said assay reagent kit comprising an assay reagent in a suitable container, said assay reagent comprising the ECL quenching moiety of claim 1 and an ECL label, and instructions for performing said method.